REMARKS

With this amendment, claims 26-36, 38-41, 43, 44, and 46-52 are pending.

Claims 26-31, 33-35, and 40 are amended. Support for the amendments to claims 26-29 may be found, for example, in original claims 26-29 and in the international application as published[1] at page 86, lines 24-25. Support for the amendments to claims 30, 31, and 33-35 may be found, for example, in original claims 30, 31, and 33-35, respectively. Support for the amendment to claim 40 may be found, for example, in the international application as published at page 33, lines 7-10.

Claims 46-52 are newly added. Support for new claims 46 and 47 may be found, for example, in original claim 30. Support for new claim 48 may be found, for example, in original claim 31. Support for new claim 49 may be found, for example, in the international application as published at page 19, lines 20-21. Support for new claim 50 may be found, for example, in original claim 33. Support for new claims 51 and 52 may be found, for example, in original claim 34.

I. Election/Restrictions

In numbered paragraph 2, under the heading "Election/Restrictions," the Office notes that claims 30 and 33-**35** are directed to non-elected species and, therefore, re withdrawn from further consideration. In the paragraph that immediately follows, the Office then states that claims 26-29, 31, 32, **35**, 36, and 38-45, to the extent that they read upon the elected species, are examined on the merits in the Office action. Thus, the Office's position on the status of claim 35 seems to be inconsistent.

While Applicant believes claim 35 to be directed to a non-elected species and, therefore, withdrawn at this time, Applicant respectfully requests the Office to clarify the same in its next communication.

II. 35 U.S.C. §112

A. Claims 40, 41, and 42

Reconsideration is requested of the rejection of claim 40 under 35 U.S.C. §112, second paragraph as being indefinite.

[1] International Publication No. WO 2004/056181.

The Office asserts that the term "blood-based" renders claim 40 indefinite. Without addressing the merits of the Office's rejection, in an effort to expedite prosecution of the application, Applicant has removed the term "blood-based" as part of the deletion of the larger phrase "blood-based or crystalloid carrier" and replaced the same with the phrase "pharmaceutically acceptable carrier, diluent, adjuvant, and/or excipient." Accordingly, the Office's rejection as applied to this claim is rendered moot.

Claims 41 and 42 were asserted to be indefinite insofar as they depend from claim 40. Accordingly, the amendment to claim 40 renders the rejection of claims 41 and 42 moot as well.

B. Claim 45

Reconsideration is requested of the rejection of claim 45 under 35 U.S.C. §112, second paragraph as being indefinite.

The Office asserts that claim 45 provides for the use of a composition or medicament, but that since the claim does not set forth any steps involved in the method or process it is unclear what method or process is intended.

With this amendment, claim 45 has been canceled. Accordingly, the rejection as applied thereto is rendered moot.

III. 35 U.S.C. §101

Reconsideration is requested of the rejection of claim 45 under 35 U.S.C. §101 as being an improper process claim.

With this amendment, claim 45 has been canceled. Accordingly, the rejection as applied thereto is rendered moot.

IV. 35 U.S.C. §103(a)

Reconsideration is requested of the rejection of claims 26-29, 31, 32, 35, 36, and 38-45 under 35 U.S.C. §103(a) as being unpatentable over Chien ("Chien (1997)")[2] in view of Berdyaev et al.[3] and Chien et al. ("Chien et al. (1994)")[4]

[2] U.S. Patent No. 5,656,420.
[3] U.S. Patent No. 5,432,053.

Initially, Applicant notes that claim 35 is believed to be directed to a non-elected species. As such, the rejection of the same would be rendered moot.

Claims 26, 27, 28, and 29 are generally directed to a method for reducing electrical disturbance of a cell's resting membrane potential, a method for reducing damage to a cell, tissue or organ following ischemia, a method for preconditioning a cell or tissue during ischaemia or reperfusion, or a method for reducing damage to a cell, organ or tissue before, during and following a surgical or clinical intervention, respectively. The methods generally comprise administering an effective amount of a composition comprising an effective amount of (i) a local anaesthetic; and (ii) at least one of a potassium channel opener, an adenosine receptor agonist, an anti-adrenergic, a calcium antagonist, an opioid, an NO donor and a sodium hydrogen exchange inhibitor, said composition further comprising a physiological potassium concentration.

Chien (1997) describes a method for employing the delta opioid DADLE to extend tissue survival time during ischemia. The opioid was added to a "Euro-Collins," "Collins M," or "University of Wisconsin" solution for use as a "preservation solution." The compositions utilized by Chien (1997) are hyperkalemic, containing concentrations of potassium above physiological concentrations. Notably, at these concentrations, the heart would be arrested by high potassium alone from depolarisation of the cell membrane.

Berdyaev et al. describe "a solution for the conservation of living organs," which contains, *inter alia*, a local anaesthetic. The components in this solution and the respective concentrations of those components in the solution are listed at column 2, lines 4 to 12. Notably, the potassium concentration disclosed in Berdyaev et al., like that disclosed in Chien (1997), is also high (at 12mM to 17mM).

Chien et al. (1994) disclose experiments to test the ability of the delta opioid DADLE to extend tissue survival time in multiorgan preservation.

The Office asserts that at "the time of the invention, a method for the preservation of tissues or cells comprising nearly all of the claimed elements was known, as taught by Chien (1997). Further, methods were known at the time of the invention for using similar compositions to preserve heart tissue and that such

[4] Journal of Thoracic and Cardiovascular Surgery, 107(3): 965-967 (1994).

compositions could comprise an anaesthetic, as taught by Chien (1994) and Berdyaev [et al.], respectively."[5] In supporting these arguments, the Office asserts that "the composition used by Chien [(1997)] comprises concentrations of ions which are similar to that of a blood-based solution." However, the compositions utilized by Chien (1997) are hyperkalemic, containing relatively high potassium concentrations – concentrations above physiological concentrations. As mentioned above, at these concentrations the heart would be arrested by high potassium alone from depolarisation of the cell membrane. Thus the composition disclosed by Chien (1997) would not be suitable for the presently claimed purposes, and one skilled in the art would not readily combine the disclosure of Chien (1997) with the "methods [that] were known."

In contrast, the composition used in the method of the present invention has physiological potassium concentrations such that when the composition is administered the cell membrane remains in a more normal physiological polarised state thereby minimising damage to the cell tissue or organ following ischemia compared to high potassium solutions. Applicant has demonstrated that good to excellent recovery of organ function is also achieved following reperfusion with the composition.[6] This is best illustrated in Example 9[7] of the present application, whereby the composition provides superior arrest, protection, and preservation in injured rat hearts compared to modified St Thomas hospital solution No. 2 which contains a high and non-physiological potassium concentration (16mM)[8]. Thus, the composition described by Chien (1997) contains high and non-physiological potassium concentrations and functions in a significantly different way compared to the composition of the present invention for reducing damage to a cell, tissue or organ following ischemia. The person skilled in the art would not have considered this reference to be relevant to the present invention. As such, one skilled in the art would not have combined it with either of Berdyaev et al. or Chien et al. (1994).

In addition, the Office asserts that "motivation to combine these teachings is provided by Berdyaev et al., who teach that anaesthetics are a desirable addition to

[5] Office action dated January 2, 2008.
[6] *See*, international application as published, at page 9, lines 10 to 11.
[7] The international application as published has two examples marked "Example 9." In this instance, Applicant is referring to the first "Example 9" which begins on page 76 at line 7.
[8] *See*, international application as published, page 79, final paragraph.

such compositions because they are useful for stabilisation of membranes (col 2, lines 28-30)."

Berdyaev et al. describes "a solution for the conservation of living organs", which contains, *inter alia*, a local anaesthetic. The potassium concentrations of the compositions disclosed in this reference are also high (at 12 to 17mM). As such, one skilled in the art would not have considered this document to be relevant to the subject invention.

Quite to the contrary, both Chien (1997) and Berdyaev et al. teach away from the claimed invention, as they disclose potassium levels that are ***above*** typical physiological levels, and that are even detrimental to the heart tissue.

Accordingly, the Office has failed to establish that claims 26, 27, 28, and 29 are obvious. Claims 31, 32, 36, and 38-45, which depend from one of claims 26, 27, 28, and 29 are patentable for the reasons stated above with respect to claims 26-19, and by reason of the additional requirement each claim requires.

CONCLUSION

In view of the foregoing, Applicants respectfully request withdrawal of the rejection of claims 40-42 and 45 under 35 U.S.C. §112, second paragraph; of claim 45 under 35 U.S.C. §101; and of claims 26-29, 31, 32, 36, and 38-45 under 35 U.S.C. §103(a), and allowance of all claims as presented herein.

Applicants request an extension of time to and including July 2, 2008, for filing a response to the above-mentioned Office action. The Commissioner is hereby authorized to charge this fee, as well as any additional fees which may be required, to Deposit Account No. 19-1345.

Respectfully submitted,

/Timothy B. McBride/

Timothy B. McBride, Reg. No. 47,781
SENNIGER POWERS LLP
One Metropolitan Square, 16th Floor
St. Louis, Missouri 63102
(314) 231-5400

TBM/VMK/sxm

Filed via EFS